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13. A method for screening compounds capable of binding to G protein-coupled receptors comprising the steps of (a) subjecting the host cell according to claim 1 to a test compound; and (b) measuring the effect of the test compound on cell growth.

14. The method according to claim 13, wherein the host cell is yeast.

15. A host cell comprising a heterologous G protein-coupled receptor, and a mutation of a host cell gene that results in an improved functional response of the G protein coupled receptor in a cell-based assay.

16. The host cell according to claim 15, wherein the mutation results in improved agonist stimulated growth promoting ability.

17. The host cell according to claim 15, wherein the mutation results in improved coupling between the heterologous G protein-coupled receptor and a heterotrimeric G protein or failure of the receptor to interact with cell desensitization or sequestration-internalization machinery, or proper plasma membrane localization.

18. The host cell according to claim 15, wherein the host cell gene encodes a regulatory receptor protein kinase, and the mutation causes a reduction in receptor phosphorylation.

19. The host cell according to claim 18, wherein the regulatory receptor protein kinase is selected from the group consisting of G protein-coupled receptor kinases, protein kinase A, protein kinase C and casein kinase.

20. The host cell according to claim 15, wherein the host cell gene encodes a component of the endocytic or degradative pathway and the mutation causes a reduction in receptor sequestration, internalization, or degradation.

21. The host cell according to claim 15, wherein the mutation affects the ratio or nature of sterols in the host cell membrane.

22. The host cell according to claim 21, wherein the host cell is yeast and the host cell gene is selected from the group consisting of *ERG2*, *ERG3*, *ERG4*, *ERG5*, and *ERG6*.

23. The host cell according to claim 22, wherein the host cell gene is *ERG6*.

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24. The host cell according to claim 23, wherein the heterologous G protein-coupled receptor is selected from the group consisting of a human melanocortin receptor, a rat somatostatin SSTR2 receptor, a rat M3 muscarinic acetylcholine receptor, and a rat CCKB receptor.

25. The host cell according to claim 21, wherein the host cell is yeast and the host cell gene is selected from the group consisting of *HEM1*, *HEM3*, *SUT1*, *PDX3*, *UPC1*, and *UPC2* (*UPC20*) and wherein the mutation allows the host cell to grow in the presence of exogenously added sterols.

26. A method for screening compounds capable of binding to G protein-coupled receptors comprising the steps of (a) subjecting the host cell according to claims 15, 18, 20, or 21 to a test compound; and (b) measuring the effect of the test compound on cell growth.

27. A method for expressing constitutively active heterologous G protein-coupled receptors in a host cell comprising:

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- (a) transforming the host cell with a vector comprising a DNA sequence encoding a modified heterologous G protein-coupled receptor, wherein the modification results in a constitutively active G protein-coupled receptor; and
  - (b) culturing the transformed host cell to permit expression of the heterologous G protein-coupled receptor.

28. The method according to claim 27, wherein the host cell is yeast.

29. A host cell comprising a modified G protein alpha subunit gene, wherein the modified G protein alpha subunit gene encodes a chimeric G alpha protein.

30. The host cell according to claim 29, wherein the host cell is a eukaryotic cell.

31. The host cell according to claim 30, wherein the host cell is yeast.

32. The host cell according to claim 29, wherein the modified G protein alpha subunit gene comprises a first nucleic acid sequence encoding the amino terminal domain of an endogenous G alpha protein, linked to a second nucleic acid sequence encoding the carboxy terminus of a heterologous G alpha protein.

33. The host cell according to claim 29, wherein the modified G protein alpha subunit gene comprises a substitution of a first nucleic acid sequence encoding the five carboxy terminal amino acids of an endogenous G alpha protein for a second nucleic acid sequence encoding the five carboxy terminal amino acid sequences of a heterologous G alpha protein.

34. The host cell according to claim 32, wherein the amino terminal domain of the G alpha protein comprises an interaction domain for a G beta protein, a G gamma protein, and an effector molecule.

35. The host cell according to claim 32 or 33, wherein the modified G protein alpha subunit gene is *GPA1*.

36. The host cell according to claim 32 or 33, further comprising a heterologous G protein-coupled receptor.

37. The host cell according to claim 36, wherein the modified G protein alpha subunit gene is *GPA1* and the host cell is yeast.

38. The host cell according to claim 36, wherein the heterologous G alpha protein is a mammalian protein.

39. The host cell according to claim 37, wherein the modified *GPA1* gene comprises a first nucleic acid sequence encoding the amino terminal domain of an endogenous G alpha protein, linked to a second nucleic acid sequence encoding the carboxy terminus of a mammalian G alpha protein selected from the group consisting of  $G\alpha i2$ ,  $G\alpha i3$ ,  $G\alpha o$ ,  $G\alpha s$ ,  $G\alpha q$ ,  $G\alpha z$ ,  $G\alpha 11$ ,  $G\alpha 12$ ,  $G\alpha 13$ ,  $G\alpha 14$ ,  $G\alpha 15$ , and  $G\alpha 16$ .

40. The host cell according to claim 37, wherein the modified *GPA1* gene comprises a substitution of a first nucleic acid sequence encoding the five carboxy terminal amino acids of an endogenous G alpha protein for a second nucleic acid sequence encoding the five carboxy terminal amino acid sequences of a mammalian G alpha protein selected from the group consisting of  $G\alpha i2$ ,  $G\alpha i3$ ,  $G\alpha o$ ,  $G\alpha s$ ,  $G\alpha q$ ,  $G\alpha 11$ ,  $G\alpha z$ ,  $G\alpha 12$ ,  $G\alpha 13$ ,  $G\alpha 14$ , and  $G\alpha 15$ , and  $G\alpha 16$ .

41. The host cell according to claim 36, wherein the heterologous G protein-coupled receptor is selected from the group consisting of rat somatostatin SSTR2, rat adenosine A2a, rat muscarinic acetylcholine M2 and M3, *D. melanogaster* muscarinic

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acetylcholine M1, rat neurotensin NT-1, human vasopressin V2, rat cholecystokinin CCK-A and CCK-B, human gonadotropin releasing hormone GnRH, human melanocortin MCR4, human adrenergic  $\alpha 2A$ , *Aplysia californica* octopamine OA1, human bombesin receptor related sequence 3 (BRS3), human histamine H3, and human  $\beta 2$ -adrenergic receptor.

42. An isolated DNA sequence encoding a chimeric G alpha protein, wherein the DNA sequence comprises a first nucleic acid sequence encoding the amino terminal domain of a G alpha protein of a first species, and a second nucleic acid sequence encoding the carboxy terminus of a G alpha protein of a second species, which is different from the first species.

43. The DNA sequence according to claim 42, wherein the amino terminal domain of the G alpha protein of the first species comprises an interaction domain for a G beta protein, for a G gamma protein, and for an effector molecule.

44. An isolated DNA sequence encoding a chimeric G alpha protein, wherein a first nucleic acid sequence encoding the five carboxy terminal amino acids of a G alpha protein from a first species is substituted for a second nucleic acid sequence encoding the five carboxy terminal amino acid sequences of a G alpha protein from a second species, which is different from the first species.

45. A polypeptide encoded by the DNA claim 42 or 44.

46. A method of measuring agonist-stimulated activation of a heterologous G protein-coupled receptor in a host cell comprising:

- (a) transforming the host cell according to claim 29 with a vector comprising a DNA sequence encoding a heterologous G protein-coupled receptor;
- (b) culturing the transformed host cell in the presence of an agonist specific for the heterologous G protein-coupled receptor; and
- (c) measuring the growth of the host cell in response to the agonist to determine the agonist-stimulated activation of the heterologous G protein-coupled receptor.

47. A method of measuring the coupling specificity of a G alpha protein for a heterologous G protein-coupled receptor comprising:

- (a) transforming a host cell according to claim 29 with a vector comprising a DNA sequence encoding a heterologous G protein-coupled receptor;
- (b) culturing the transformed host cell in the presence of an agonist specific for the heterologous G protein-coupled receptor; and
- (c) measuring the growth of the host cell in response to the agonist to determine the coupling specificity of the G alpha protein for the heterologous G protein-coupled receptor.

48. The method according to claims 46 or 47, wherein the host cell is yeast.

49. A method of measuring agonist-stimulated activation of a heterologous G protein-coupled receptor in a host cell comprising:

- (a) culturing a host cell according to claim 36 in the presence of an agonist specific for the heterologous G protein-coupled receptor; and
- (b) measuring the growth of the host cell in response to the agonist to determine the

agonist-stimulated activation of the heterologous G protein-coupled receptor.

50. A method of measuring the coupling specificity of a G alpha protein for a heterologous G protein-coupled receptor comprising:

- (a) culturing a host cell according to claim 36 in the presence of an agonist specific for the heterologous G protein-coupled receptor; and
- (b) measuring the growth of the host cell in response to the agonist to determine the coupling specificity of the G alpha protein for the heterologous G protein-coupled receptor.

51. The method according to claim 49 or 50, wherein the host cell is yeast.

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